ORAL CONTRIBUTIONS

822

Treatment of In-Stent Restenosis

Monday, March 08, 2004, 4:00 p.m.-5:30 p.m.
Morial Convention Center, La Nouvelle C

4:00 p.m.

822-1 Oral Sirolimus to Inhibit Recurrent In-Stent Stenosis: The Randomized, Double-Blind, Placebo-Controlled OSIRIS Trial

Jörg Hausleiter, Adnan Kastrati, Julinda Mehilli, Helmut Schühlen, Franz Dotzer, Christoph Goos, Gisela Pogatsa-Murray, Michael Vogeser, Martin Breuer, Josef Dirschinger, Albert Schömig, The OSIRIS Study Group, German Heart Center Munich, Munich, Germany, 1. Medizinische Klinik, Klinikum rechts der Isar, Munich, Germany

Sirolimus coated stents are a promising new therapy for restenosis in de-novo coronary lesions. Except for the promising results achieved with brachytherapy, the treatment of recurrent in-stent-restenosis (ISR) remains a challenging clinical issue. Given the efficacy of systemic administration of Sirolimus to prevent neointimal hyperplasia in animal models and to halt and even reverse the progression of allograft vasculopathy, it seems reasonable to consider this drug as a good option for oral treatment to prevent recurrent ISR. This randomized, double-blind, placebo-controlled study is aimed at evaluating the efficacy of 2 different regimens of oral Sirolimus in patients with ISR treated with repeat PTCA. We enrolled 300 patients with ISR in native coronary arteries who were randomly assigned to one of three treatment arms: usual-dose Sirolimus, high-dose Sirolimus and placebo. All patients in the two treatment arms received Sirolimus loading two days prior to and the day of intervention followed by maintenance therapy for 7 days. The difference between usual- and high-dose arms was in the amount of pre-treatment, 8 mg in the usual-dose Sirolimus arm and 24 mg in the high-dose Sirolimus arm. The maintenance therapy after intervention consisted of 2mg/d for 7 days in both arms. Angiographic binary restenosis at 6-months angiography was the primary end point of the study. Sample size was estimated to give sufficient power to the trial for detecting a 25 and 50% reduction of the binary restenosis with the two Sirolimus doses. Angiographic and 1-year clinical follow-up is in progress and will be completed in January 2004. The final study results will be presented.

4:15 p.m.

822-2 Is Sirolimus-Eluting Stent Better Than Brachytherapy to Treat In-Stent Restenosis at Longer (12-Month) Follow-Up? Angiographic and Intravascular Ultrasound Analysis

Fausto Feres, Juan S. Muñoz, Alexandre Abizaid, Rodolfo Staico, Luiz A. Mattos, Galo Maldonado, Marinella Centemero, Ibraim Pinto, Andrea S. Abizaid, Aurea Chaves, Luiz F. Tanajura, Amanda Sousa, J. Eduardo Sousa, Institute Dante Pazzanese of Cardiology, Sao Paulo, Brazil

We have previously reported the comparison between Intracoronary Beta-Radiation Therapy (BT) and Sirolimus-eluting stent (SES) to treat in-stent restenosis (ISR) at 6-month follow-up.
Purpose: To report 12-month of clinical, angiographic and intravascular ultrasound (IVUS) outcomes of patients (Pts) with ISR treated either with balloon angioplasty followed by BT or SES.
Methods: Fifty consecutive pts with ISR were treated either with SES or BT (Novoste, Beta-Cath). The first 25 Pts were treated with SES and the second 25 Pts treated with BT (40 mm source). Clinical, angiographic and IVUS analysis were performed in all pts at baseline (Post), at 6 and 12-month follow-up (FUP).
Results: Demographics characteristics were similar in both groups. 100% of SES group and 80% of the BT group were free of major adverse cardiac events [MACE (death, myocardial infarction, or re-intervention)] at 6-month after procedure (p=0.05). At 12-month FUP, 96% of SES and only 64% of BT group were free of MACE (p=0.01). Angiographic and IVUS results are shown below.

Angiographic Results (mm)	SES (n=25)	BT (n=25)	*P*
In-lesion length	13.66±7.80	18.66±4.17	0.006
Reference Diameter Post	2.8±0.36	2.72±0.36	0.4
MLD Pre	1.05±0.31	1.06±0.33	0.9
MLD in-segment Post	2.35±0.37	1.95±0.26	<0.0001
MLD in-stent Post	2.72±0.31	1.98±0.26	<0.0001
Acute gain	1.67±0.34	0.91±0.39	<0.0001
MLD in-segment, 12-month	2.19±0.56	1.47±0.43	<0.0001
MLD in-stent, 12-month	2.36±0.57	1.64±0.55	<0.0001
Late loss in-segment	0.16±0.42	0.48±0.32	0.004
Late loss in-stent	0.35±0.45	0.34±0.46	0.9
Angiographic restenosis, 6-month	1(4%)	4(16%)	0.3
Angiographic restenosis, 12-month	1(4%)	8(32%)	0.02
Intimal Hyperplasia(mm^3),12-month	1.76±3.44	38.7±7.88	<0.0001

Conclusions: SES group presented better acute and late sustained angiographic results (larger MLD post, FUP and lower late loss), consequently, restenosis rate and MACE were significantly smaller in the SES group.

4:30 p.m.

822-3 Sirolimus-Eluting Stents for Failed Brachytherapy: Results From the SECURE Registry

Paul S. Teirstein, Theodore A. Bass, Marco A. Costa, Steven Yakubov, Andrew J. Carter, Jeffrey W. Moses, Martin B. Leon, Roxanna Mehran, Matthew J. Price, Tim A. Fischell, Scripps Clinic Research Foundation, La Jolla, CA

Background: Brachytherapy is currently the only modality with proven efficacy for instent restenosis (ISR), but failure rates approximate 25%. The sirolimus-eluting Bx VELOCITY™ stent has shown promising results for de novo coronary stenosis, however its efficacy in the setting of ISR and failed brachytherapy is unknown.
Methods: Sirolimus-eluting stents were implanted under a compassionate use protocol in patients who were high risk for ISR and had failed previous intervention. Patients were treated at 5 study sites: Scripps Clinic, Lenox Hill Hospital, the University of Florida Jacksonville Health Science Center, Riverside Methodist Hospital, and the Providence Health System. All patients with failed BT had mandated 8 month follow up angiography.
Results: See table.
Conclusions: Stent thrombosis was infrequent in radiation failure patients receiving sirolimus stents. At 6 month follow-up, target lesion revascularization in radiation failure patients receiving sirolimus stents is low, and similar to non-radiation failure patients. Sirolimus stents are a safe and effective treatment for vascular radiation failure.

SECURE - Events In & Out of Hospital to 6 months

	Radiation Failure (n=146 pts)	No Radiation Failure (n=56 pts)	P-value
Death (%)	1.4	1.8	NS
MI (%)	2.7	0	NS
Q-wave	0.7	0	NS
Non-Q wave	2.1	0	NS
MACE (death, MI, TLR)	12.3	8.9	NS
TLR (%)	11.6	5.4	NS
TVR (%)	11.6	5.4	NS
Stent thrombosis <30 days (%)	0.7	0	NS
Stent thrombosis >30 days (%)	1.4*	0	NS
*One pt had thrombosis during f/u IVUS			

4:45 p.m.

822-4 Intravascular Ultrasound Follow-Up of the SECURE Trial: The Compassionate Use of Sirolimus-Elutings Stents Study

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Background –Little is known about the vascular effects of drug-eluting stents in patients with ISR who already failed radiation therapy and bypass surgery. The aim of this study was to determine the vascular effects of SES in patients enrolled in the SECURE trial using 3D volumetric intravascular ultrasound. Methods: The compassionate use of SES (SECURE) trial was conducted in 5 clinical US sites. All patients with failed brachytherapy had scheduled 8 month IVUS follow-up. Volumetric 3D IVUS data was analyzed by an independent core lab. Methods and Results – 252 patients have been enrolled in the SECURE trial. So far, 39 patients have completed 8-month IVUS follow-up. Mean age was 60 y, 66% were male, 78% had previous CABG, 35% were diabetics and 16% had SVG lesions. On average, 1.38 stents/lesion were implanted. Mean stented segment length was 27.4mm. Overall, lumen volume after 8-months was 155mm^3 and there was 10.1% intimal hyperplasia. Minimal lumen CSA was 4.14mm^2. Eleven patients had >50% lumen obstruction by IVUS. There was no stent malapposition or aneurysm formation at follow-up. Only one patient showed positive vessel remodeling at follow-up. Matched baseline and follow-up data (table). Conclusion –The use of SES in patients with previous radiation therapy was not associated with stent malapposition or significant vessel remodeling or aneurysm formation. The IH volume after SES was minimal and compares favorably with that observed in a much lower risk population treated with bare stents.

N=10	Total Vessel mm^3	Plaque mm^3	Lumen mm^3	%NIH
Post	412	235	177	0
Follow-up	396	233	163	11.8%